ORIGINAL PAPER

OPTIMAL CONCENTRATIONS IN THE ENZYME REACTIONS

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Abstract. *This paper contains a particular point of view about the solution of an optimal control problem. The subject is the enzymatic reaction modeled as a dynamical system, when a disturbing external factor is present.*

Keywords: *enzyme, optimal, solution.*

1. INTRODUCTION

The first proposed enzymatic reaction in the literature is the reaction between substrate *S* and enzyme *E* to give complex product *SE* then converted in *P* product and *E* enzyme. General mechanism is the conversion of the substrate *S* by the enzyme *E*, as a catalyst, to the product *P*. The resulting from Mass Action Law is that the rate of reaction depends on the product concentrations of reactants.

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SE \to P + E \tag{1}$$

Concentrations of reactants are marked with lowercase letters, as follows [7]:

$$s = [S],\ e = [E],\ c = [SE],\ p = [P]$$

Then, according to the Law of Mass Action (the rate of a reaction is proportional to the product of the concentrations of the reactants), the previous equation leads to the following nonlinear system:

$$\begin{aligned} \dot{s} &= -k_1 es + k_{-1} c \\ \dot{e} &= -k_1 es + (k_{-1} + k_2) c \\ \dot{c} &= k_1 es - (k_{-1} + k_2) c \\ \dot{p} &= k_2 c \end{aligned} \tag{2}$$

We have denoted by k_1, k_{-1}, k_2 the constant parameters associated to the reaction rates. To complete the mathematical formulation, the initial conditions are necessary:

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$$s(0)=s_0,\ e(0)=e_0,\ c(0)=c_0,\ p(0)=p_0$$

The solutions of this system give the concentrations, consequently the rates of the reactions, as functions of time.

Our contribution is to study this mathematical model, in a simple mode, in order to obtain an optimal solution, under the influence of an external factor. We shall denote by M. S. A.(method of obtaining the analytical solution), the semi-invert method based on Kalman's theory, to obtain the analytical formula and the graphical representation of the trajectory and optimal control for a class of control problems.

This method can be applied in Kalmans theory ([1]) to any pair of square matrices, *A(t)* and *B(t)*, and for any initial inputs. Dynamical system Σ will have the following general form:

$$f(x,t,u)=A(t)x(t)+B(t)u(t) \tag{3}$$

$$y(t)=C(t)x(t) \tag{4}$$

where: *A(t)* is the system matrix, *B(t)* is the command matrix, *u(t, x)* is the command (the vector of inputs), *y(t)* is the answer, and *x(t)* the state vector, *t* the time variable, *f(x, u, t)* is a self-adjoint operator, in the finite dimensional case, a symmetric, positive matrix (in the finite dimensional case *A(t), B(t), C(t)* are also symmetric and positive matrices).

Correspondingly, the spaces that own these variables are: state space *X*, space output *Y*, space of admissible commands *U*, all of them n-dimensional, Hilbert spaces.

Optimal control problem is limited to determining the control *u(t)* which minimizes the quadratic cost function for any initial pair $(t_0,x_0)\in(T_1,T_2)\times X$. If $z:(T_1,T_2)\to L(X,X)$ is continuously differentiable then $u(t,x)=\frac{1}{2}\langle x,z(x)x\rangle$ is, according to Kalman's theory, also continuously differentiable. Also according to Kalman's theory, if found a Hamilton Jacobi solution $u(t,x)$, then the optimal control problem can be solved. It shows that $z(\cdot)$ is the solution of a Riccati type equation formed by the Σ system coefficients [2-6].

$$\dot{z}=-z*A(t)-A*z(t)+z*Q(t)z(t)-\rho(t) \tag{5}$$

where: $Q(t)=B(t)\cdot\sigma^{-1}(t)\cdot B*(t)$, $\rho(t)$ is a continuous application and $\sigma(t)$ is regular on (T_1,T_2).

2. BASIC ENZYME REACTION MODELED AS DYNAMICAL SYSTEM

The system matrix *A* is diagonalized according to equation (1). We shall replace the nonlinear terms, *es*, as dependent values of *s*, *e* and *c*, dependency related in a different way for each equation, as follows:

$$c=k_0\cdot s,\ es=k\cdot s,\ es=k_3\cdot e,\ c=k_{-2}\cdot e,\ es=k_{-3}\cdot c$$

We do not take into account the last equation, taking into account that there is only one dependency that's p of c, so we retain only the first three relationships. The result, rewritten by the state variables, will be as follows:

$$\begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \end{pmatrix} = \begin{pmatrix} K_1 & 0 & 0 \\ 0 & K_2 & 0 \\ 0 & 0 & K_3 \end{pmatrix} \cdot \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} \tag{6}$$

with nonzero determinant. To find the optimal control, that is in order to achieve the optimal product concentration se, we will use the dynamic system associated to the previously presented mathematical model [2-6].

We have denoted:

$$x_1 = s,\ x_2 = e,\ x_3 = c,$$
$$K_1 = k_{-1}k_0 - k_1 k,\ K_2 = k_{-2}\left(k_{-1} + k_2\right) - k_1 k_3,\ K_3 = k_1 k_{-3} - \left(k_{-1} + k_2\right)$$

The dynamic system will be as follows [7]:

$$\begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \end{pmatrix} = \begin{pmatrix} K_1 & 0 & 0 \\ 0 & K_2 & 0 \\ 0 & 0 & K_3 \end{pmatrix} \cdot \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} + \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} \cdot \begin{pmatrix} u \\ 0 \\ 0 \end{pmatrix} \tag{7}$$

$$y = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix} \cdot \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} \tag{8}$$

with:

$$A = \begin{pmatrix} K_1 & 0 & 0 \\ 0 & K_2 & 0 \\ 0 & 0 & K_3 \end{pmatrix},\ B = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

in which u is the command applied to the first component s of the concentrations vector: *se*.

3. AN ANALYTICAL SOLUTION FOR THE BASIC ENZYME REACTION OPTIMAL CONTROL PROBLEM

In the considered example, we have the restrictions:

$$\sigma = 1,\ \rho = 0,\ A = A^*,\ B = B^*,\ u(t,x) = (u,0,0),\ t_0 = 0,\ t_1 = 1$$

In consequence, we can form the Bernoulli equation, having sufficient condition that *A* and *B* to be symmetric, positive matrices and $\det(A + A^*) \neq 0$, which is true.

$$\dot{z}(t) + (A + A^*) \cdot z(t) - B^2 z^2(t) = 0_2$$

with:

$$z(t_1) = z(1) = e^A$$

with the solution:

$$z(t) = \left[B_2 \cdot (A + A^*)^{-1} - e^{(A+A^*)t} \cdot -e^{-2 \cdot A - A^*} + e^{-A-A^*} \cdot B^2 \cdot (A + A^*)^{-1}\right]^{-1}$$

The resultant optimal command will have the following analytical formula:

$$u(t, x) = -B \cdot z(t) \cdot x(t)$$

where *x(t)* is :

$$x(t) = x_0 \cdot e^{\int_0^t [A - B^2 \cdot z(\nu)] d\nu}$$

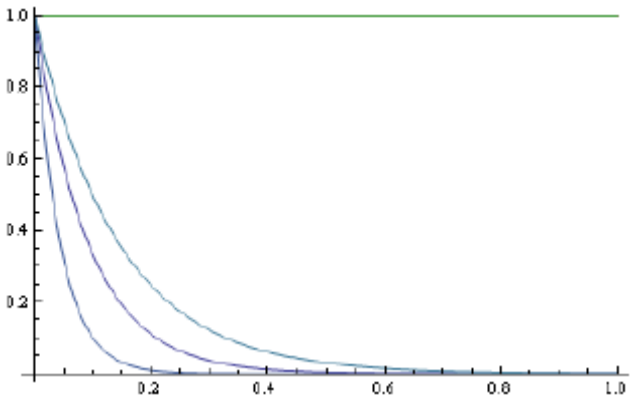
with: $x_0 = (s_0, e_0, 0)$. Also:

$$x(t) = (s(t), e(t), c(t))$$

So, knowing the analytical expression of the component *c(t)*, and returning to the original system of four equations yields:

$$z(t) = k_2 \int_0^t c(\nu) d\nu$$

Graphic behavior of the three factors that ultimately determine the resulting product, is presented in the figure below:



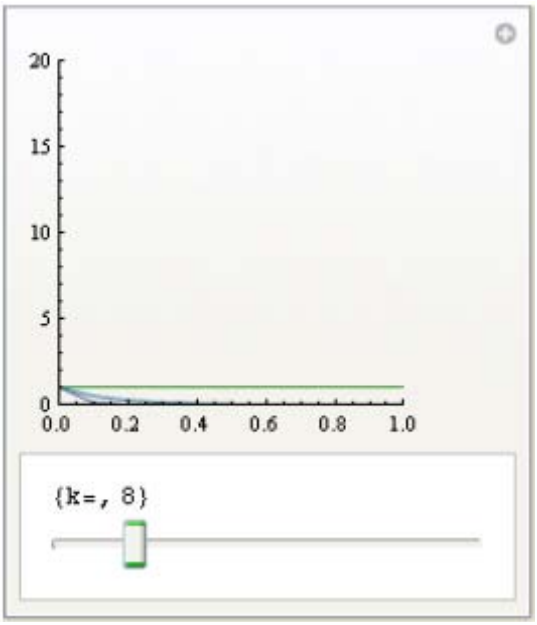


Fig. 1. The behavior of the components, *s, e, c*, depending on time, required for the product of concentration *k = 8*.

Corresponding source code for arbitrary values $k_1 = 1$, $k_2 = 3$, $k_3 = 5$, $k_{-1} = 6$, $k_{-2} = 2$, $k_{-3} = 2$, $k_0 = 1$, using "Mathematica 6.0" is in the file: "Enzyme reactions.nb", which leads to different graphical representations, in relation to behavior change parameter values of *k*:

```
        Manipulate[Column[
"k=", k, Slider[Dynamic[k], 1, 40, 1]
            ],Delimiter,Row[Dynamic[ Plot[x, t, 0, 20, AspectRatio
        → 1, PlotRange → 0, 1, 0, 20], SynchronousUpdating → True]]]
```

4. CONCLUSIONS

Mention that the process used in calculations, makes possible, in most cases, to introduce a number of interactive practically unlimited of parameters, and allows analysis of a large number of examples. The method can determine the analytical formula and numerical results, also the graphical behavior of the three concentrations expected in the reactions, for most of the cases.

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